REMARKS

The Examiner rejected in the Office Action claims 39-40 and 45-57 and objected to claims 41-44. The Applicants respond to the rejections and objections in the order the Examiner presented them.

The Objection to Claims 40-41

The Examiner objected that Claim 40 recites an inhibitor that "binds the" VEGFR-3 catalytic domain instead of "binds to the" domain. The Applicants have amended the claim in the manner the Examiner suggested; they point out that its meaning and scope is unchanged, as "binding a protein" is a well-established, though perhaps less-preferred, alternative for "binding to a protein."

The Examiner objected that Claim 41 recites an indolinone "selected from" various indolinones and stated that it should recite "selected from the group consisting of," instead. The Applicants have amended the claim in the manner the Examiner suggested, but point out that "selected from the group consisting of" is only "[o]ne acceptable form of alternative expression" (MPEP § 2173.05(h)), and that "selected from," without "the group consisting of," is also proper.

The Enablement Rejection Under 35 § 112, First Paragraph

The Examiner rejected claims 39-40 and 45-57 under 35 U.S.C. § 112, first paragraph, arguing that the specification does not enable a method of extending corneal graft survival using "*any* 'VEGFR-3 kinase inhibitor,'" "any anti-angiogenic agent," and "*any* immunosuppressive agent." Office Action, at 2-3 (emphasis in original); the Examiner frames the issue this way again at 5. The Applicants respectfully disagree that this rejection is proper.

First, the issue is not whether the Applicants have enabled a method using "*any* VEGFR-3 kinase inhibitor" (although the Applicants maintain that they have). The pending claims are not directed to "any" inhibitor, but are directed, instead, to a method using a pharmaceutical composition comprising an "*indolinone* [VEGFR-3]

kinase inhibitor." The Applicants' invention is broader than that, and the specification describes more, but all of the pending claims require indolinones. When the Examiner argues that the specification does not enable the claims because, for example, the specification does not provide the chemical structure of "*all* 'VEGFR-3 kinase inhibitor[s]'" (Office Action, at 6; emphasis in original), the Examiner is arguing against the enablement of claims not at issue here. What matters is whether the specification enables the *pending* claims, all of which require indolinones.

Second, enablement does not require that the Applicants expressly identify "any and all" possible indolinone VEGFR-3 inhibitors, as the Examiner maintains. *See* Office Action, at 3. The Examiner indirectly states the correct test for enablement: the question is whether, in view of the specification, one can practice the claimed invention without undue experimentation. M.P.E.P. 2164.01. But to meet this standard a specification need not disclose "any and all" embodiments that may fall within the scope of the claims. One can arrive at them through experimentation: even "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Colianni*, F.2d 220, 224, 195 U.S.P.Q. 150, 153 (CCPA 1977).

The specification meets this test. As the Examiner points out, the specification discloses three indolinone VEGFR-3 kinase inhibitors, MAE87, MAE106, and MAZ51. Moreover, the specification describes methods for identifying more:

> VEGFR-3 kinase inhibitors useful in the invention include specific VEGFR-3 kinase inhibitors such as indolinones that differentially block VEGF-C and VEGF-D induced VEGFR-3 kinase activity compared to that of VEGFR-2 . . . Additional VEGFR-3 kinase inhibitors, including specific, selective and non-selective inhibitors, are known in the art or can be identified using one of a number of well known methods for assaying for receptor tyrosine kinase inhibition.

> As an example, a VEGFR-3 kinase inhibitor can be identified using a well known ELISA assay to analyze production of phosphorylated tyrosine . . . Such an assay can be used to screen for molecules that inhibit VEGFR-3 in preference to other vascular endothelial growth factor receptors such as VEGFR-1 and in preference to unrelated tyrosine kinases such as fibroblast growth factor receptor1 (FGFR1).

Specification, at ¶¶ 43-44. The specification then describes the steps needed to perform the assay.

The specification states that the "assay can be used to screen for molecules that inhibit VEGFR-3," at ¶ 44, and here, the case is even simpler: one is not screening *all* molecules, but only a very specific class of molecules, indolinones. Of course, one will probably have to experiment to identify the indolinones that work best. But the skill of the art here is quite high (those who practice it usually have advanced degrees and extensive knowledge); the experimentation required is simple and routine, involving well-known assays and methods; and the specification provides guidance as to which molecules work best – the indolinones required by the claims. The Applicants respectfully submit that, in view of these factors, the experimentation required here is not undue. The specification, as a result, enables the claims.

The same can be said of the dependent claims: practicing the method they claim does not require undue experimentation. The Examiner argues that the specification does not enable one to use an anti-angiogenic agent and immunosuppressive agent in connection with the indolinones of the claims. But the specification describes several anti-angiogenic agents at paragraphs 77 – 81, and describes several immunosuppressive agents at paragraphs 82-84. This puts one of ordinary skill in the art (and, again, the level of skill in the art here is quite high) in a position to identify additional anti-angiogenic and immunosuppressive agents without undue experimentation.

For the foregoing reasons, the Applicants respectfully submit that the claims fully comport with the requirements of §112, first paragraph, and respectfully request that the Examiner withdraw the rejection of enablement under that section.

The written description rejection under 35 § 112, first paragraph

The Examiner rejected claims 39-40 and 45-57 under 35 U.S.C. § 112, first paragraph, arguing that the specification does not reasonably provide a written description of "*any* VEGFR-3 kinase inhibitor." Office Action, at 8 (emphasis in original). The Applicants respectfully disagree that this rejection is proper.

The issue is not whether the specification describes "any VEGFR-3 kinase inhibitor" (although the Applicants maintain that it does describe them). As before, the Applicants point out that the pending claims are not directed to "*any* VEGFR-3 kinase inhibitor." They are directed, instead, to a method using a pharmaceutical composition comprising an "*indolinone* [VEGFR-3] kinase inhibitor." All of the claims require indolinones. The issue, therefore, is whether the specification describes a method using indolinone VEGFR-3 kinase inhibitors. The Applicants respectfully submit that it does.

Further, the issue is not whether the specification expressly identifies each and every indolinone that falls within the scope of the claims. The written description requirement does not require this. An applicant can satisfy the requirement by disclosing

> "relevant identifying characteristics, i.e., structure or other physical and/or chemical properties [or by disclosing] functional characteristics coupled with a known or disclosed correlation between function and structure."

M.P.E.P. § 2163(II)(A)(3)(ii). So, for example, an applicant can describe an antibody solely by describing the antigen to which it binds. *Synopsis Of Application Of Written Description Guidelines*, http://www.uspto.gov/web/menu/written.pdf (2003), at 60. One need not describe each and every antibody that binds the antigen. Describing a

particular structure (an antigen) and a desired function (binding to an antibody) is sufficient. The principal rationale underlying this result is that antibodies are well known in the art and the steps for generating them are routine.

The specification and claims at issue here comport with the written description for similar reasons. The claims are directed to methods of using indolinones that inhibit VEGFR-3. The specification discloses a chemical structure: an indolinone; and discloses a function: inhibition of VEGFR-3. The steps required to identify additional indolinones that would inhibit VEGFR-3 are well known in the art and are employed as a matter of routine. The Applicants submit that, for this reason, the specification adequately describes the claims.

The Examiner further objected that the specification does not identify "any anti-angiogenic agent" and "*any* immunosuppressive agent." The application does not have to. Instead, it describes several anti-angiogenic agents at paragraphs 77 – 81, and several immunosuppressive agents at paragraphs 82-84. This is sufficient to comport with the written description requirement.

For the foregoing reasons, the Applicants respectfully request that the Examiner withdraw the rejection under § 112, first paragraph.

The Applicants respectfully submit that the claims, as amended, are in condition for allowance. If the Examiner believes an interview would be useful for advancing the prosecution of this Application, he is invited to contact the undersigned attorney at (714) 246-4920.

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The undersigned authorizes the Director to charge any fees required or necessary for the filing, processing or entering of this paper or any of the papers transmitted with it, and to refund any overpayment, to deposit account 01-0885.

Respectfully submitted,

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